The association between a single nucleotide polymorphism in the SOCS-3 gene and caloric intake is modified by body mass index

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Introduction

- Obesity is characterized by an excess of adipose tissue in the body.
- Obesity is strongly associated with leptin resistance.
- Leptin is a crucial hormone regulating appetite and energy balance in the human body.
- Leptin is produced by the adipose tissue (adipocytes).
- Leptin resistance is associated with excessive energy intake.
- SOCS-3 (Suppressor of cytokine signaling) is a protein that inhibits leptin signalling.
- Overexpression of SOCS-3 is associated with leptin resistance.
- A single nucleotide polymorphism (SNP) lies at the -4874th nucleotide upstream from the SOCS-3 gene (rs4969170) and consists of an A to G substitution.

Objectives

1) To determine whether there is an association between the single nucleotide polymorphism (rs4969170) in the SOCS-3 gene and indices of obesity.
2) To determine if caloric intake is influenced by the rs4969170 SNP in the SOCS-3 gene.
3) To determine if the rs4969170 SNP in the SOCS-3 gene modifies the association between indices of obesity (body mass index and waist circumference) and caloric intake.

Methods

Population:
- 219 University of Toronto students between the ages of 20-29.

Method:
- Dietary assessment was performed using a 196-item Food Frequency Questionnaire (FFQ).
- Height and weight were measured to calculate body mass index (BMI in kg/m²).
- Waist circumference was measured at the mid-point between the iliac crest and the lower ribs.
- Physical activity was recorded in Metabolic Equivalent Task Score (METS) - leisure and occupational activity only.
- Genotyping was completed using Real-time PCR with high resolution melt function using ECO Instrument (Illumia).

Statistical Analyses

- Analysis of variance (continuous variables) or X² (sex variable) were used to test for a difference between genotypes (SOCS-3) for the general characteristics of the population including BMI and caloric intake.
- General linear models were used to test for an interaction between SOCS-3 polymorphism and indices of obesity on caloric intake adjusted for sex and physical activity.

Results

Table 1: General characteristics of the population by SOCS-3 genotype (rs4969170)

<table>
<thead>
<tr>
<th>Variable</th>
<th>SOCS-3 Genotypes</th>
<th>P</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>22.8±2.5</td>
<td>22.5±2.7</td>
</tr>
<tr>
<td>Sex (M/F %)</td>
<td>25/26</td>
<td>43/42</td>
</tr>
<tr>
<td>WC¹ (cm)</td>
<td>75.2±9.7</td>
<td>73.7±8.7</td>
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<tr>
<td>Physical Activity² (METS)</td>
<td>1.9±0.4</td>
<td>1.7±0.4</td>
</tr>
</tbody>
</table>

¹Waist Circumference
²Metabolic Equivalent Task Score

Figure 1: Association between SOCS-3 polymorphism (rs4969170) and body mass index (kg/m²). The analysis was adjusted for sex and physical activity.

Figure 2: Association between SOCS-3 polymorphism (rs4969170) and caloric intake (kcal). The analysis was adjusted for sex and physical activity.

Figure 3: Body mass index (median - kg/m²) modifies the association between SOCS-3 polymorphism (rs4969170) and caloric intake (kcal). P = 0.007 for interaction adjusted for sex and physical activity.

Conclusions

- The rs4969170 SNP in the SOCS-3 gene does not have a significant influence on BMI or Caloric Intake when analyzed individually.
- When BMI (or waist circumference), caloric intake and genotype are analyzed jointly, a unique relationship for the AG genotype is observed.
- Among individuals with the AG genotype, having a lower BMI is associated with a greater caloric intake whereas having a larger BMI is associated with a smaller caloric intake.
- Blood leptin levels and other polymorphisms in the SOCS-3 gene must be examined to further understand this relationship.
- These findings may have implications for individualized obesity prevention strategies.

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